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TERMINAL (ENTER 1, 2, 3, OR ?):2


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=> s cilobradine
L1 23 CILOBRADINE

```
=> s l1 and (myocardial or hypertrophy)
L2          15 L1 AND (MYOCARDIAL OR HYPERTROPHY)

=> s l2 and treat
=> s l2 and treat?
  16 FILES SEARCHED...
L3          15 L2 AND TREAT?

=> s l1 and (beta(a)blocker)
L4           8 L1 AND (BETA(A) BLOCKER)

=> dis l3 1-15 bib abs

L3   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:780659  CAPLUS
DN   135:335152
TI   Use of bradycardiac substances in the treatment of
     myocardial diseases associated with hypertrophy and
     novel drug combinations
IN   Daemmgen, Juergen; Guth, Brian; Seidler, Randolph
PA   Boehringer Ingelheim Pharma K.-G., Germany
SO   PCT Int. Appl., 13 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   WO 2001078699       A2     20011025    WO 2001-EP4034          20010407
     WO 2001078699       A3     20020620
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     DE 10018401         A1     20011025    DE 2000-10018401        20000413
     CA 2404120          AA     20011025    CA 2001-2404120         20010407
     EP 1276476          A2     20030122    EP 2001-949281          20010407
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     TR 200202326        T2     20030321    TR 2002-200202326       20010407
     BR 2001009996       A      20030527    BR 2001-9996            20010407
     JP 2003535050       T2     20031125    JP 2001-576000          20010407
     EE 200200590        A      20040415    EE 2002-590             20010407
     BG 107103           A      20030430    BG 2002-107103          20020913
     ZA 2002008162       A      20031017    ZA 2002-8162            20021010
     NO 2002004924       A      20021011    NO 2002-4924            20021011
     US 2004014795       A1     20040122    US 2003-257481          20030613
PRAI DE 2000-10018401    A      20000413
     WO 2001-EP4034      W      20010407
AB   The invention relates to a novel use of bradycardiac substances such as a
     Ca++ channel blocker, beta-receptor blockers or if channel blockers, the
     if channel blockers being preferred.  The substances are optionally used
     in combination with a cardio-active substance for inducing the regression
     of myocardial diseases associated with hypertrophy, in
     particular for treating idiopathic hypertrophic cardiomyopathies
     (HCM) in humans and domestic animals.  Thus 1.25 mg cilobradine
     was encapsulated in capsules that were prepared from 82.75 mg lactose
     monohydrate and 55.3 mg corn starch.
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L3 ANSWER 2 OF 15 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10507592 IFIPAT;IFIUDB;IFICDB
TI USE OF BRADYCARDIAC SUBSTANCES IN THE **TREATMENT** OF **MYOCARDIAL** DISEASES ASSOCIATED WITH **HYPERTROPHY** AND NOVEL MEDICAMENT COMBINATIONS
INF Daemmgen; Juergen, Ochsenhausen, DE
Guth; Brian, Warthausen, DE
Seidler; Randolph, Biberach, DE
IN Daemmgen Juergen (DE); Guth Brian (DE); Seidler Randolph (DE)
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877, US
PI US 2004014795 A1 20040122
AI US 2003-257481 20030613
WO 2001-EP4034 20010407
20030613 PCT 371 date
20030613 PCT 102(e) date
PRAI DE 2000-100184014 20000413
FI US 2004014795 20040122
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 8
AB The present invention relates to the new use of bradycardiac substances such as a Ca++ channel blocker, beta-receptor blocker or if channel blocker, the if channel blockers being preferred, optionally in combination with a cardioactive substance for inducing the regression of **myocardial** diseases accompanied by **hypertrophy**, particularly for the **treatment** of idiopathic hypertrophic cardiomyopathies (HCM) in humans and domestic pets.
CLMN 8

L3 ANSWER 3 OF 15 USPATFULL on STN
AN 2004:233875 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, UNITED STATES
Swindell, Charles E., Merion, PA, UNITED STATES
Webb, Nigel L., Bryn Mawr, PA, UNITED STATES
Bradley, Matthews O., Laytonsville, MD, UNITED STATES
PA Protarga, Inc., King of Prussia, PA (U.S. corporation)
PI US 2004180949 A1 20040916
AI US 2003-618884 A1 20030714 (10)
RLI Continuation of Ser. No. US 2001-846838, filed on 1 May 2001, GRANTED, Pat. No. US 6602902 Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, ABANDONED Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, GRANTED, Pat. No. US 5795909
DT Utility
FS APPLICATION
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in **treating** noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 15 USPATFULL on STN
AN 2004:179136 USPATFULL

TI Use of a specific cyclic amine derivative or the pharmaceutically acceptable salts thereof for the **treatment** or prevention of heart failure
IN Guth, Brian, Warthausen, GERMANY, FEDERAL REPUBLIC OF
Seidler, Randolph, Sandy Hook, CT, UNITED STATES
Daemmgen, Juergen, Oschenhausen, GERMANY, FEDERAL REPUBLIC OF
PA Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
PI US 2004138306 A1 20040715
AI US 2003-626138 A1 20030724 (10)
PRAI EP 2002-16602 20020725
US 2002-405915P 20020826 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 676
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides the use in a pharmaceutical composition of a specific cyclic amine derivative, or its pharmaceutically acceptable salts, for the **treatment** or prevention of heart failure of any aetiology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 15 USPATFULL on STN
AN 2004:139413 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, UNITED STATES
Bradley, Matthews O., Laytonsville, MD, UNITED STATES
Swindell, Charles S., Merion, PA, UNITED STATES
Shashoua, Victor E., Brookline, MA, UNITED STATES
PA Protarga Pharmaceuticals, Inc., King of Prussia, PA (U.S. corporation)
PI US 2004106589 A1 20040603
AI US 2003-455250 A1 20030605 (10)
RLI Continuation of Ser. No. US 2000-730450, filed on 5 Dec 2000, GRANTED, Pat. No. US 6576636 Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2524
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in **treating** noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 15 USPATFULL on STN
AN 2004:19491 USPATFULL
TI Use of bradycardiac substances in the **treatment** of **myocardial** diseases associated with **hypertrophy** and novel medicament combinations
IN Daemmgen, Juergen, Ochsenhausen, GERMANY, FEDERAL REPUBLIC OF
Guth, Brian, Warthausen, GERMANY, FEDERAL REPUBLIC OF
Seidler, Randolph, Biberach, GERMANY, FEDERAL REPUBLIC OF

PI US 2004014795 A1 20040122
AI US 2003-257481 A1 20030613 (10)
WO 2001-EP4034 20010407
PRAI DE 2000-10018401 20000413
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P. O. BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 238
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the new use of bradycardiac substances such as a Ca.sup.++ channel blocker, beta-receptor blocker or i.sub.f channel blocker, the i.sub.f channel blockers being preferred, optionally in combination with a cardioactive substance for inducing the regression of **myocardial** diseases accompanied by **hypertrophy**, particularly for the **treatment** of idiopathic hypertrophic cardiomyopathies (HCM) in humans and domestic pets.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 15 USPATFULL on STN
AN 2003:85867 USPATFULL
TI Oral delivery formulation
IN Compton, Bruce Jon, Lexington, MA, UNITED STATES
Solari, Nancy E., West Newton, MA, UNITED STATES
Flangan, Margaret A., Stow, MA, UNITED STATES
PI US 2003059471 A1 20030327
AI US 2001-997277 A1 20011129 (9)
RLI Continuation of Ser. No. US 1998-55560, filed on 6 Apr 1998, ABANDONED
PRAI US 1997-69501P 19971215 (60)
US 1998-73867P 19980204 (60)
DT Utility
FS APPLICATION
LREP Stephen J Gaudet, 68H Stiles Road, Salem, NH, 03079
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Flakes containing drugs and methods for forming and using such flakes are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 15 USPATFULL on STN
AN 2002:17328 USPATFULL
TI Dha-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor, Brookline, MA, UNITED STATES
Swindell, Charles, Merion, PA, UNITED STATES
Webb, Nigel, Bryn Mawr, PA, UNITED STATES
Bradley, Matthews, Layton, PA, UNITED STATES
PI US 2002010208 A1 20020124
US 6602902 B2 20030805
AI US 2001-846838 A1 20010501 (9)
RLI Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, ABANDONED
Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, GRANTED, Pat. No. US 5795909
DT Utility
FS APPLICATION
LREP Edward R. Gates, Esq., Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210

CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in **treating** noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 15 USPATFULL on STN
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
US 6576636 B2 20030610
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2511
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in **treating** noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 15 USPATFULL on STN
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in **treating** cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 15 USPAT2 on STN

AN 2002:17328 USPAT2
TI Dha-pharmaceutical agent conjugates to improve tissue selectivity
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles E., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Layton, PA, United States
PA Protarga, Inc., King of Prussia, PA, United States (U.S. corporation)
PI US 6602902 B2 20030805
AI US 2001-846838 20010501 (9)
RLI Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, now abandoned Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, now patented, Pat. No. US 5795909
DT Utility
FS GRANTED
EXNAM Primary Examiner: Krass, Frederick; Assistant Examiner: Jagoe, Donna
LREP Wolf, Greenfield, & Sacks, P.C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in **treating** noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 15 USPAT2 on STN
AN 2001:90260 USPAT2
TI Method of **treating** a liver disorder with fatty acid-antiviral agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PA Protarga, Inc., King of Prussia, PA, United States (U.S. corporation)
PI US 6576636 B2 20030610
AI US 2000-730450 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and antiviral agents useful in **treating** liver disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 15 WPINDEX COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-204046 [20] WPINDEX
DNC C2004-080618
TI Use of cyclic amine derivative in the preparation of composition for **treating** or preventing heart failure due to e.g. **myocardial** infarction.
DC B02 B07
IN DAEMMGEN, J; GUTH, B; SEIDLER, R
PA (BOEH) BOEHRINGER INGELHEIM PHARMA GMBH & CO KG
CYC 1

PI CA 2435526 A1 20040125 (200420)* EN 73
ADT CA 2435526 A1 CA 2003-2435526 20030718
PRAI EP 2002-16600 20020725
AN 2004-204046 [20] WPINDEX
AB CA 2435526 A UPAB: 20040324
NOVELTY - In the preparation of a composition for the **treatment** or prevention of heart failure, a cyclic amine derivative (I/I'), its enantiomer, diastereomer, N-oxide or salt is used.

DETAILED DESCRIPTION - In the preparation of a composition for the **treatment** or prevention of heart failure, a cyclic amine derivative of formula (I) or (I'), its enantiomer, diastereomer, N-oxide or salt is used.

R1 = R2, CF3, nitro, amino, 1-3C alkylamino or 1-3C dialkylamino;

R2 = H, halo, OH, 1-3C alkoxy, 1-3C phenylalkoxy or 1-3C alkyl;

R1+R2 = 1-2C alkylenedioxy;

E = 1-3C straight-chain alkylene (optionally substituted by 1-3C alkyl);

A = -CH2-CH2-, -CH=CH-, -CH2-CO-, -NH-CO-, -CO-CO- or -CHOH-CO-;

B = -CH2-CH2, -CH2CO- or -CH2CS-;

G = 1-4C straight-chain alkylene (optionally substituted by 1-3C alkyl) or -G1-G2-

G1 = 2-4C straight chain alkylene (optionally substituted by 1-3C alkyl) attached to N;

G2 = oxa, thia, (methyl)imino, sulfinyl or sulfonyl (all attached to R);

R = phenyl (substituted by R3, R4 and R5);

R3 = H, halo, 1-3C alkyl, 1-3C alkoxy, OH, nitro, CN, or CF3;

R4 = H, alkoxy, 1-3C alkylsulfonyloxy, amino, 1-3C (di)alkylamino, or 2-3C alkanoylamino;

R3+R4 = 1-2C alkylenedioxy;

R5 = H, halo, OH, 1-3C alkyl, or 1-3C alkoxy;

m = 1 - 5;

n = 0 - 2;

m+n = 3 - 5;

A' = -CH2-, -CH2-CH2-, or -CH=CH-;

B' = -CH2-, -CH2-CH2-, -CO- or -CH2CO-;

G' = 1-6C straight chain alkylene (optionally substituted by 1-3C alkyl) or -G'1-G'2-;

G'1 = 2-5C straight-chain alkylene (optionally substituted by 1-3C alkyl) attached to N;

G'2 = oxa, thia, sulfinyl, sulfonyl, or imino (optionally substituted by 1-3C alkyl) attached to R';

m' = 1 - 6;

n' = 0 - 3;

m'+n' = 3 - 6;

R' = 5- membered heteroaryl containing O, S and/or 1-2N, or 6-membered heteroaryl containing 1 - 2 N (both optionally mono- or di-substituted by halo, alkyl, OH, (phenyl)alkoxy, Ph, dimethoxyphenyl, nitro, amino, acetylamino, carbamoylamino, N-alkylcarbamoylamino, hydroxymethyl, (alkyl)mercapto, alkylsulfinyl, alkylsulfonyl, alkylsulfonyloxy, alkylsulfonylamino, alkoxycarbonylmethoxy, carboxymethoxy, methylenedioxy, or ethylenedioxy (where imino group in the ring is substituted by alkyl, phenylalkyl or Ph)), indolyl (optionally substituted by benzyl, benzyloxy, benzylamino (all optionally mono- to tri-substituted by methoxy or methyl), (di)methylamino, methoxy, acetoxy, CF3, trichloromethyl, carboxy, methoxycarbonyl, ethoxycarbonyl, CN, cyclohexyl, trimethoxyphenyl, trihalophenyl, dihaloaminophenyl) or naphthyl (optionally substituted by 1-2C alkylenedioxy, or mono- or disubstituted by halo, alkyl, OH, alkoxy, alkylsulfonyloxy, nitro, amino or alkanoylamino), benzyloxy, 4,5,6,7-tetrahydrobenzo(b)thienyl or phenyl (optionally substituted by 1-2C alkylenedioxy, halo, alkyl, OH, alkoxy, phenylalkoxy, nitro, amino, alkanoylamino, alkylsulfonylamino, bis(alkylsulfonyl)amino, alkylsulfonyloxy, CF3, trifluoromethoxy, trifluoromethylsulfonyloxy, or disubstituted by halo, alkyl, or alkoxy, trialkoxyphenyl, tetraalkylphenyl or dihaloaminophenyl.

Provided that:

(a) when A is -CH2-CH2-, -CH=CH-, -CH2CO- or -NH-CO- then B is -CH2-CH2-, -CH2CO- or CH2CS-; or when A = -CO-CO- or -CHOH-CO- then B is -CH2-CH2-;

(b) when B' is -CH2- or -CO-, then R' is also chosen from phenyl (optionally substituted by 1-2C alkylenedioxy, halo, alkyl, OH, alkoxy, phenylalkoxy, nitro, amino, alkanoylamino, alkylsulfonylamino, bis(alkylsulfonyl)amino, alkylsulfonyloxy, CF3, trifluoromethoxy, trifluoromethylsulfonyloxy or disubstituted by halo, alkyl, or alkoxy, trialkoxyphenyl, tetraalkylphenyl or dihaloaminophenyl.

ACTIVITY - Cardiant; Cardiovascular-Gen; Hypotensive; Respiratory-Gen; Thrombolytic; Antiarrhythmic.

An experiment was carried out to compare visual side effect of the test compound (Cilobradine) and a control (Zatebradine). The reduction of heart rate was measured after the administration of chosen doses. A reduction of 75 % of the heart rate is obtained with test while a reduction of 44 % of the heart rate is obtained with control.

MECHANISM OF ACTION - Hyperpolarization activated cation current channel (HCN) blocker.

USE - For the treatment or prevention of heart failure (claimed) of aetiology diagnosed as a consequence or complication of any other condition , disease or disorder e.g. cardiac insufficiency, cardiac failure, heart insufficiency, myocardial failure, myocardial insufficiency, heart muscle insufficiency, cardiac muscle insufficiency, insufficient cardiac output, heart muscle weakness, cardiac collapse, cardiac syncope, chronic heart failure, acute heart failure, heart decompensation, cardial decompensation, diastolic heart failure, right sided heart failure, systolic heart failure, left ventricular heart failure, left sided heart failure, biventricular heart failure, congestive heart failure, systolic dysfunction, diastolic dysfunction, ischemic heart diseases, including myocardial infarction, right ventricular infarction, chronic ischemia, coronary heart diseases, hypertension, primary pulmonary hypertension, secondary pulmonary hypertension, pulmonary embolism, pulmonary arterial stenosis, chronic obstructive pulmonary disease, restrictive cardiomyopathies, dialated cardiomyopathies due to infectious, toxic, metabolic, familial or unknown reasons, myocarditis, congenital anomalies, tachycardias and ventricular hypertrophy secondary to genetic or volvular disorders such as tricuspid valve insufficiency, mitral and/or aortic valve disorders, heart infarcts, thyroid diseases and anemia.

ADVANTAGE - The compound exhibits pharmacologically longer duration of action, dose for dose potency and cardioselectivity, resulting in decreased or absent side effects.

Dwg.0/3

L3 ANSWER 14 OF 15 WPINDEX COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-111133 [12] WPINDEX
DNC C2004-045298
TI Use of **cilobradine** or its salt for the **treatment** or prevention of heart failure such as cardiac insufficiency, cardiac failure.
DC B02
IN DAEMMGEN J DBH & CO, KG; GUTH B
DBH & CO, KG; SEIDLER R UBH & CO, KG; DAEMMGEN, J; GUTH, B; SEIDLER, R
PA (BOEH) BOEHRINGER INGELHEIM PHARMA GMBH & CO KG
CYC 106
PI EP 1362590 A1 20031119 (200412)* EN 15
R: AL AT BE CH CY CZ DE DK EE ES FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
EP 1362590 B1 20040107 (200412) EN
R: AL AT BE CH CY CZ DE DK EE ES FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
WO 2004011006 A1 20040205 (200413) EN
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC
VN YU ZA ZM ZW

EP 1362590 A8 20040225 (200416) EN

R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC NL
PT RO SE SI SK TR

DE 60200160 E 20040212 (200419)

ES 2211846 T3 20040716 (200447)

US 2004138306 A1 20040715 (200447)

AU 2003254554 A1 20040216 (200453)

ADT EP 1362590 A1 EP 2002-16602 20020725; EP 1362590 B1 EP 2002-16602 20020725; WO 2004011006 A1 WO 2003-EP7929 20030721; EP 1362590 A8 EP 2002-16602 20020725; DE 60200160 E DE 2002-00200160 20020725, EP 2002-16602 20020725; ES 2211846 T3 EP 2002-16602 20020725; US 2004138306 A1 Provisional US 2002-405915P 20020826, US 2003-626138 20030724; AU 2003254554 A1 AU 2003-254554 20030721

FDT DE 60200160 E Based on EP 1362590; ES 2211846 T3 Based on EP 1362590; AU 2003254554 A1 Based on WO 2004011006

PRAI EP 2002-16602 20020725

AN 2004-111133 [12] WPINDEX

AB EP 1362590 A UPAB: 20040218

NOVELTY - In the preparation of a pharmaceutical composition for the **treatment** or prevention of heart failure, a **cilobradine** (A1) or its salt is used.

ACTIVITY - Cardiant; Vasotropic; Cardiovascular-Gen.; Hypotensive; Thrombolytic; Respiratory-Gen.; Antithyroid; Antianemic.

MECHANISM OF ACTION - None given.

USE - In the preparation of a pharmaceutical composition for the **treatment** or prevention of heart failure (claimed) such as cardiac insufficiency, cardiac failure, heart insufficiency, **myocardial** failure, **myocardial** insufficiency, heart muscle insufficiency, cardiac muscle insufficiency, insufficient cardiac output, heart muscle weakness, cardiac muscle weakness, cardiac collapse, cardiac syncope, chronic heart failure, acute heart failure, heart decompensation, cardiac decompensation, cardial decompensation, diastolic heart failure, right sided heart failure, systolic heart failure, left ventricular heart failure, left sided heart failure, biventricular heart failure and congestive heart failure; for the **treatment** of heart failure of any aetiology means heart failure diagnosed as a consequence or complication of any other condition, disease or disorder such as systolic dysfunction, diastolic dysfunction, ischemic heart diseases, including **myocardial** infarction, right ventricular infarction and chronic ischemia, coronary heart diseases, hypertension, primary pulmonary hypertension, secondary pulmonary hypertension, pulmonary embolism, pulmonary arterial stenosis, chronic obstructive pulmonary disease, restrictive cardiomyopathies, dilated cardiomyopathies due to infectious, toxic, metabolic, familial or unknown reasons, myocarditis, congenital anomalies, tachycardias and ventricular **hypertrophy** secondary to genetic or valvular disorders such as tricuspid valve insufficiency, mitral and aortic valve disorders, heart infarcts, thyroid diseases and anemia.

ADVANTAGE - (A1) provides an advantage over zatebradine not only in terms of its pharmacologically longer duration of action and dose for dose potency, but more importantly in its cardioselectivity resulting in decreased or absent visual side effects when compared to therapeutic doses of zatebradine. (A1) has intrinsically different pharmacological properties than zatebradine, which permit full cardiac ion channel blockade with absent or diminished retinal effects. (A1) able to reduces the mortality and morbidity associated with heart failure of any aetiology.

Dwg.0/3

L3 ANSWER 15 OF 15 WPINDEX COPYRIGHT 2004 THE THOMSON CORP on STN

AN 2002-011919 [02] WPINDEX
DNC C2002-003158
TI Medicament for **treating hypertrophy**-related **myocardial** disease, containing bradycardic agent, preferably **cilobradine**, and optionally another cardiac drug.
DC B02
IN DAEMMGEN, J; GUTH, B; SEIDLER, R; DAMMGEN, J
PA (BOEH) BOEHRINGER INGELHEIM PHARMA KG; (BOEH) BOEHRINGER INGELHEIM PHARMA GMBH & CO KG; (DAEM-I) DAEMMGEN J; (GUTH-I) GUTH B; (SEID-I) SEIDLER R
CYC 96
PI DE 10018401 A1 20011025 (200202)* 5
WO 2001078699 A2 20011025 (200202) GE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001070484 A 20011030 (200219)
NO 2002004924 A 20021011 (200304)
EP 1276476 A2 20030122 (200308) GE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
SK 2002001458 A3 20030304 (200321)
KR 2002089453 A 20021129 (200322)
CZ 2002003752 A3 20030312 (200324)
BR 2001009996 A 20030527 (200344)
CN 1422153 A 20030604 (200356)
HU 2003000917 A2 20030828 (200363)
JP 2003535050 W 20031125 (200380) 18
US 2004014795 A1 20040122 (200407)
ZA 2002008162 A 20031231 (200408) 28
MX 2002009935 A1 20030201 (200413)
ADT DE 10018401 A1 DE 2000-10018401 20000413; WO 2001078699 A2 WO 2001-EP4034 20010407; AU 2001070484 A AU 2001-70484 20010407; NO 2002004924 A WO 2001-EP4034 20010407, NO 2002-4924 20021011; EP 1276476 A2 EP 2001-949281 20010407, WO 2001-EP4034 20010407; SK 2002001458 A3 WO 2001-EP4034 20010407, SK 2002-1458 20010407; KR 2002089453 A KR 2002-713688 20021011; CZ 2002003752 A3 WO 2001-EP4034 20010407, CZ 2002-3752 20010407; BR 2001009996 A BR 2001-9996 20010407, WO 2001-EP4034 20010407; CN 1422153 A CN 2001-807959 20010407; HU 2003000917 A2 WO 2001-EP4034 20010407, HU 2003-917 20010407; JP 2003535050 W JP 2001-576000 20010407, WO 2001-EP4034 20010407; US 2004014795 A1 WO 2001-EP4034 20010407, US 2003-257481 20030613; ZA 2002008162 A ZA 2002-8162 20021010; MX 2002009935 A1 WO 2001-EP4034 20010407, MX 2002-9935 20021008
FDT AU 2001070484 A Based on WO 2001078699; EP 1276476 A2 Based on WO 2001078699; SK 2002001458 A3 Based on WO 2001078699; CZ 2002003752 A3 Based on WO 2001078699; BR 2001009996 A Based on WO 2001078699; HU 2003000917 A2 Based on WO 2001078699; JP 2003535050 W Based on WO 2001078699; MX 2002009935 A1 Based on WO 2001078699
PRAI DE 2000-10018401 20000413
AN 2002-011919 [02] WPINDEX
AB DE 10018401 A UPAB: 20020109
NOVELTY - A medicament (A) for **treating myocardial** diseases associated with **hypertrophy** contains a bradycardic agent (I) and optionally another cardiac drug (II).

ACTIVITY - Cardiant.

In tests in a cat having severe hypertrophic cardiomyopathy, oral administration of **cilobradine** (Ia) twice daily at 0.3 mg/kg marked reduced the clinical symptoms (e.g. by reducing pain and normalizing the ECG) and also caused regression of the **myocardial hypertrophy** after 1 and 2 years.

MECHANISM OF ACTION - Calcium ion channel blocker; beta -receptor blocker; if channel blocker.

USE - (A) is used for **treating myocardial**

diseases associated with **hypertrophy** (claimed), especially idiopathic hypertrophic cardiomyopathy such as **hypertrophy** of the remaining myocardium after cardiac infarction, ischemic cardiomyopathy, valve-associated **hypertrophy** of the myocardium or myocarditis due to toxic or iatrogenic effects.

ADVANTAGE - As well as alleviating the clinical symptoms, (A) causes regression of the above severe heart conditions. if Channel blockers (I) inhibit rebound increase in cardiac frequency, and have a synergistic effect in combination with (II).

Dwg.0/0

```
=> dis hist

     (FILE 'HOME' ENTERED AT 12:42:28 ON 16 NOV 2004)

     FILE 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, DISSABS, EMA, IFIPAT,
     JICST-EPLUS, PASCAL, PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH,
     USPATFULL, USPAT2, WPIFV, WPINDEX, WTEXTILES' ENTERED AT 12:42:39 ON 16
     NOV 2004
L1            23 S CILOBRADINE
L2            15 S L1 AND (MYOCARDIAL OR HYPERTROPHY)
L3            15 S L2 AND TREAT?
L4             8 S L1 AND (BETA(A)BLOCKER)

=> s beta(a)blocker
L5         34305 BETA(A) BLOCKER

=> s l5 and (myocardial or hypertrophy)
L6          8381 L5 AND (MYOCARDIAL OR HYPERTROPHY)

=> s l6 and treat?
  20 FILES SEARCHED...
L7          6134 L6 AND TREAT?

=> dis hist

     (FILE 'HOME' ENTERED AT 12:42:28 ON 16 NOV 2004)

     FILE 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, DISSABS, EMA, IFIPAT,
     JICST-EPLUS, PASCAL, PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH,
     USPATFULL, USPAT2, WPIFV, WPINDEX, WTEXTILES' ENTERED AT 12:42:39 ON 16
     NOV 2004
L1            23 S CILOBRADINE
L2            15 S L1 AND (MYOCARDIAL OR HYPERTROPHY)
L3            15 S L2 AND TREAT?
L4             8 S L1 AND (BETA(A)BLOCKER)
L5         34305 S BETA(A)BLOCKER
L6          8381 S L5 AND (MYOCARDIAL OR HYPERTROPHY)
L7          6134 S L6 AND TREAT?

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
```

```
FULL ESTIMATED COST                                    103.16      103.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE       TOTAL
                                                       ENTRY     SESSION
CA SUBSCRIBER PRICE                                    -0.70       -0.70

STN INTERNATIONAL LOGOFF AT 12:51:01 ON 16 NOV 2004


Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1623kxg

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS  4  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS  5  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS  6  SEP 27   STANDARDS will no longer be available on STN
 NEWS  7  SEP 27   SWETSCAN will no longer be available on STN
 NEWS  8  OCT 28   KOREAPAT now available on STN
 NEWS  9  NOV 18   Current-awareness alerts, saved answer sets, and current
                   search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                   and SOLIDSTATE reloads

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:22:16 ON 23 NOV 2004

=> file reg
COST IN U.S. DOLLARS                              SINCE FILE       TOTAL
                                                       ENTRY     SESSION
FULL ESTIMATED COST                                     0.21        0.21
```

FILE 'REGISTRY' ENTERED AT 12:22:48 ON 23 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6
DICTIONARY FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6

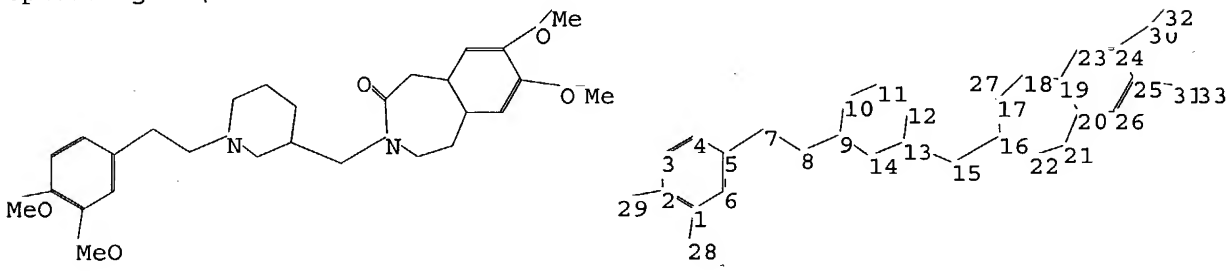
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading c:\10257481.str



chain nodes :
7 8 15 27 28 29 30 31 32 33
ring nodes :
1 2 3 4 5 6 9 10 11 12 13 14 16 17 18 19 20 21 22 23 24 25 26

chain bonds :
1-28 2-29 5-7 7-8 8-9 13-15 15-16 17-27 24-30 25-31 30-32 31-33
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-14 10-11 11-12 12-13 13-14 16-17 16-22
17-18 18-19 19-20 19-23 20-21 20-26 21-22 23-24 24-25 25-26
exact/norm bonds :
8-9 9-10 9-14 10-11 11-12 12-13 13-14 15-16 16-17 16-22 17-18 17-27
18-19 19-20 19-23 20-21 20-26 21-22 23-24 24-25 24-30 25-26 25-31
exact bonds :
1-28 2-29 5-7 7-8 13-15 30-32 31-33
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:CLASS 28:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS

```
L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l1 exact
SAMPLE SEARCH INITIATED 12:23:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA EXA SAM L1

=> s l1 sss sam
SAMPLE SEARCH INITIATED 12:23:32 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      3 TO ITERATE

100.0% PROCESSED       3 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

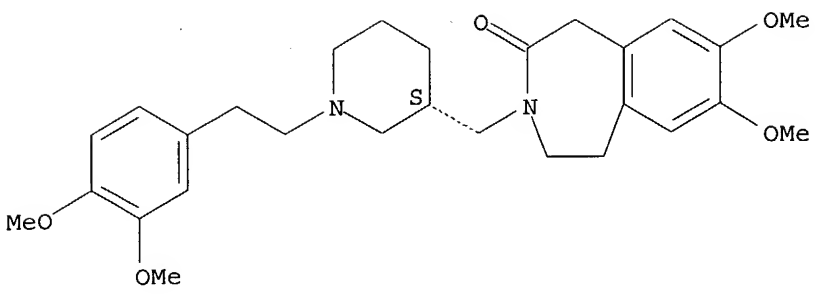
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               1 TO       80

L3            1 SEA SSS SAM L1

=> d scan

L3    1 ANSWERS   REGISTRY  COPYRIGHT 2004 ACS on STN
IN    2H-3-Benzazepin-2-one, 3-[[(3S)-1-[2-(3,4-dimethoxyphenyl)ethyl]-3-
      piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy-, monohydrochloride
      (9CI)
MF    C28 H38 N2 O5 . Cl H

Absolute stereochemistry.  Rotation (+).
```



● HCl

ALL ANSWERS HAVE BEEN SCANNED

=> s l1 sss full
FULL SEARCH INITIATED 12:23:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 62 TO ITERATE

100.0% PROCESSED 62 ITERATIONS 14 ANSWERS
SEARCH TIME: 00.00.01

L4 14 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.84	156.05

FILE 'CAPLUS' ENTERED AT 12:24:02 ON 23 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Nov 2004 VOL 141 ISS 22
FILE LAST UPDATED: 22 Nov 2004 (20041122/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4 and (myocardial or hypertrophy)
15 L4
56047 MYOCARDIAL
2 MYOCARDIALS
56048 MYOCARDIAL
(MYOCARDIAL OR MYOCARDIALS)
23414 HYPERTROPHY

```
           80 HYPERTROPHIES
        23455 HYPERTROPHY
                (HYPERTROPHY OR HYPERTROPHIES)
L5          5 L4 AND (MYOCARDIAL OR HYPERTROPHY)

=> s l5 and treat?
      3115794 TREAT?
L6          4 L5 AND TREAT?

=> dis l6 1-4 bib abs hitstr

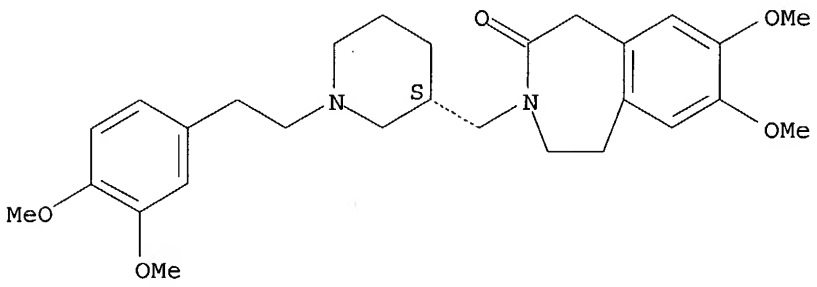
L6   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:780659  CAPLUS
DN   135:335152
TI   Use of bradycardiac substances in the treatment of
     myocardial diseases associated with hypertrophy and
     novel drug combinations
IN   Daemmgen, Juergen; Guth, Brian; Seidler, Randolph
PA   Boehringer Ingelheim Pharma K.-G., Germany
SO   PCT Int. Appl., 13 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2001078699       A2     20011025    WO 2001-EP4034         20010407
     WO 2001078699       A3     20020620
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     DE 10018401         A1     20011025    DE 2000-10018401       20000413
     CA 2404120          AA     20011025    CA 2001-2404120        20010407
     EP 1276476          A2     20030122    EP 2001-949281         20010407
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     TR 200202326        T2     20030321    TR 2002-200202326      20010407
     BR 2001009996       A      20030527    BR 2001-9996           20010407
     JP 2003535050       T2     20031125    JP 2001-576000         20010407
     EE 200200590        A      20040415    EE 2002-590            20010407
     BG 107103           A      20030430    BG 2002-107103         20020913
     ZA 2002008162       A      20031017    ZA 2002-8162           20021010
     NO 2002004924       A      20021011    NO 2002-4924           20021011
     US 2004014795       A1     20040122    US 2003-257481         20030613
PRAI DE 2000-10018401    A      20000413
     WO 2001-EP4034      W      20010407
AB   The invention relates to a novel use of bradycardiac substances such as a
     Ca++ channel blocker, beta-receptor blockers or if channel blockers, the
     if channel blockers being preferred.  The substances are optionally used
     in combination with a cardio-active substance for inducing the regression
     of myocardial diseases associated with hypertrophy, in
     particular for treating idiopathic hypertrophic cardiomyopathies
     (HCM) in humans and domestic animals.  Thus 1.25 mg cilobradine was
     encapsulated in capsules that were prepared from 82.75 mg lactose
     monohydrate and 55.3 mg corn starch.
IT   147541-45-5, Cilobradine
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (use of bradycardiac substances in treatment of
```

myocardial diseases associated with **hypertrophy** and novel drug combinations)

RN 147541-45-5 CAPLUS

CN 2H-3-Benzazepin-2-one, 3-[[(3S)-1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:481232 CAPLUS

DN 123:102317

TI Specific bradycardic agents - a novel approach to the **treatment** of **myocardial** ischemia

AU Wetzel, Bernd

CS Dr. Karl Thomae GmbH, Biberach, D-7950, Germany

SO Trends Med. Chem. '90, Proc. Int. Symp. Med. Chem., 11th (1992), 257-64. Editor(s): Sarel, Shalom; Mechoulam, Raphael; Agranat, Israel. Publisher: Blackwell, Oxford, UK.
CODEN: 60TTAQ

DT Conference

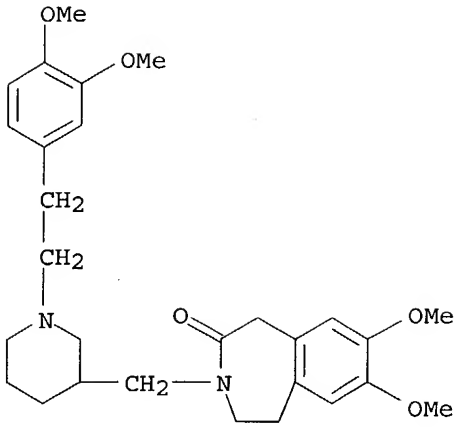
LA English

AB The specific bradycardic agents, e.g. UL-FS 49 and DK-AH 3 decreased heart rate and prolonged diastole with no or minor effects on blood pressure, and **myocardial** contractility, conduction velocity or refractoriness in animals and humans. The potential application of these agents to the **treatment** of heart ischemia and angina may have distinct advantages over other regimens, since the beneficial effect of reduced heart rate is retained without loss of ventricular contractility or without other neg. effects.

IT **109859-50-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(specific bradycardic agents - a novel approach to **treatment** of **myocardial** ischemia)

RN 109859-50-9 CAPLUS

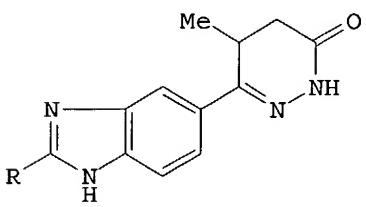
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:526606 CAPLUS
DN 113:126606
TI Benzimidazoles with an antiischemial activity on the heart, and in combinations with beta-blockers or bradycardiacs
IN Daemmgen, Juergen; Seewaldt, Elke; Trach, Volker; Psiorz, Manfred; Reiffen, Manfred; Austel, Volkhard
PA Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 330052	A2	19890830	EP 1989-102505	19890214
	EP 330052	A3	19910612		
	EP 330052	B1	19931215		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	DE 3805635	A1	19890907	DE 1988-3805635	19880224
	AT 98488	E	19940115	AT 1989-102505	19890214
	JP 01254627	A2	19891011	JP 1989-45052	19890223
PRAI	DE 1988-3805635	A	19880224		
	EP 1989-102505	A	19890214		

OS MARPAT 113:126606
GI



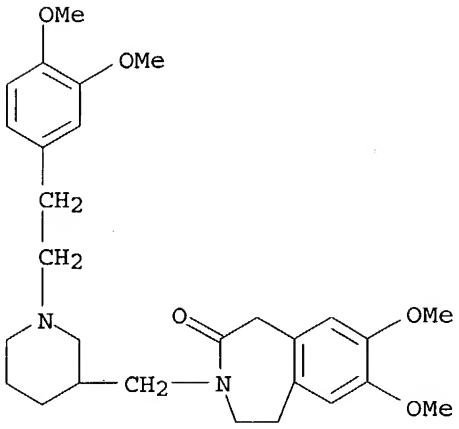
I

AB The benzimidazoles I (R = alkyl, HOC6H4, MeOC6H4) are cardiac antiischemics and also active are tautomers, salts and enantiomers of I. Compns. comprising I and a β-blocking or brachycardiac agent are synergistic drugs for the prevention or **treatment** of acute cardiac infarction. In rabbits with ligature-induced heart ischemia, 0.5 mg I (R = MeOC6H4)/kg reduced the extent of **myocardial** infarction. This effect was enhanced by the simultaneous administrtation of 0.3 mg Atenolol/kg. Formulation examples are given.

IT **129323-98-4**
RL: BIOL (Biological study)
(cardiac infarction prevention and **treatment** by)
RN 129323-98-4 CAPLUS
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy-, mixt. with 4,5-dihydro-6-[2-(4-methoxyphenyl)-1H-benzimidazol-5-yl]-5-methyl-3(2H)-pyridazinone (9CI) (CA INDEX NAME)

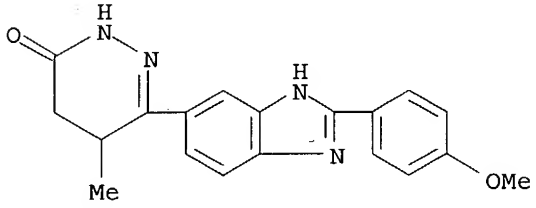
CM 1

CRN 109859-50-9
CMF C28 H38 N2 O5



CM 2

CRN 74150-27-9
CMF C19 H18 N4 O2

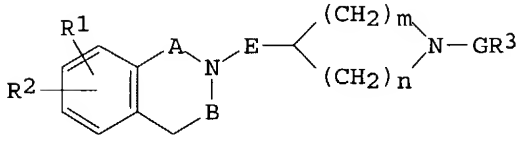


L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:496608 CAPLUS
DN 107:96608
TI Preparation of new cyclic amines as antiischemia and antitachycardia agents
IN Psiorz, Manfred; Heider, Joachim; Bomhard, Andreas; Reiffen, Manfred; Hauel, Norbert; Noll, Klaus; Narr, Berthold; Lillie, Christian; Kobinger, Walter; Daemmgen, Juergen
PA Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 29 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 3

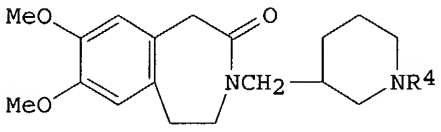
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	DE 3541811	A1	19870604	DE 1985-3541811	19851127
	SU 1442073	A3	19881130	SU 1986-4028479	19861111
	EP 224794	A2	19870610	EP 1986-116002	19861118
	EP 224794	A3	19881019		
	EP 224794	B1	19900912		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 56447	E	19900915	AT 1986-116002	19861118
	FI 8604785	A	19870528	FI 1986-4785	19861125
	FI 88299	B	19930115		
	FI 88299	C	19930426		
	DD 256132	A5	19880427	DD 1986-296626	19861125
	IL 80758	A1	19910131	IL 1986-80758	19861125
	CA 1321194	A1	19930810	CA 1986-523713	19861125
	DK 8605683	A	19870528	DK 1986-5683	19861126
	DK 174564	B1	20030610		
	JP 62138491	A2	19870622	JP 1986-281636	19861126
	JP 06025128	B4	19940406		
	HU 43056	A2	19870928	HU 1986-4901	19861126
	HU 196787	B	19890130		
	ZA 8608933	A	19880727	ZA 1986-8933	19861126
	NO 168034	B	19910930	NO 1986-4744	19861126
	NO 168034	C	19920108		
	AU 8665764	A1	19870604	AU 1986-65764	19861127
	AU 589712	B2	19891019		
	US 5175157	A	19921229	US 1991-725855	19910703
PRAI	DE 1985-3541811	A	19851127		
	EP 1986-116002	A	19861118		
	US 1986-934277	B1	19861124		
	DE 1987-3717561	A	19870525		
	US 1988-170185	B1	19880318		
	US 1988-197064	B1	19880520		
	US 1988-259228	B1	19881017		
	US 1989-426922	B1	19891024		
	US 1989-438279	B1	19891116		
	US 1990-552352	B2	19900712		
	US 1991-638001	B2	19910104		

GI



I



II

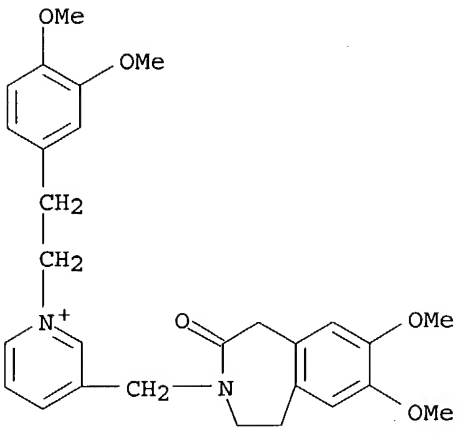
AB The title compds. [I; A = CH2CH2, CH:CH, CH2CO, COCO, CH(OH)CO, NHCO; B = CH2, CO, CS; E, G = alkylene; R1 = H, alkyl, halo, OH, (phenyl)alkoxy; R2 = CF3, NO2, amino, R1; R1R2 = alkylenedioxy; R3 = (un)substituted Ph; m = 1-5; n = 0-2; m + n = 3-5] were prepared as agents for **treatment** of **myocardial** ischemia (no data) and tachycardia. 3-(Hydroxymethyl)piperidine was N-benzylated and brominated and used to N-alkylate 1,3-dihydro-7,8-dimethoxy-2H-3-benzazepin-2-one. The product was hydrogenated to give tetrahydrobenzazepinone II (R4 = H). The latter was N-alkylated with 3,4-(MeO)2C6H3CH2CH2Br to give II [R4 = 3,4-(MeO)2C6H3CH2CH2] (III). In rats 5.0 mg III/kg i.v. reduced heart frequency 208 beats/min. Tablets were prepared each containing III 7.5,

cornstarch 59.5, lactose 48.0, polyvinylpyrrolidone 4.0, and Mg stearate 1.0 mg.

IT **109859-87-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)

RN 109859-87-2 CAPLUS

CN Pyridinium, 1-[2-(3,4-dimethoxyphenyl)ethyl]-3-[(1,2,4,5-tetrahydro-7,8-dimethoxy-2-oxo-3H-3-benzazepin-3-yl)methyl]-, bromide (9CI) (CA INDEX NAME)

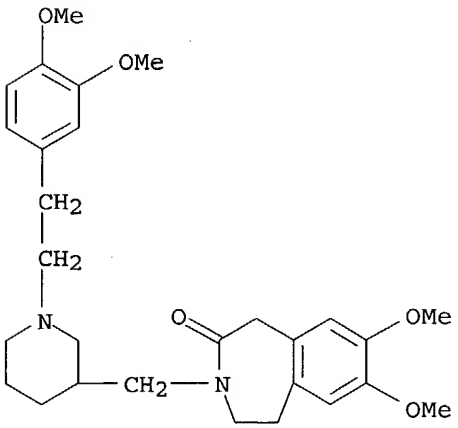


● Br^-

IT **109859-50-9P 109859-52-1P 109859-57-6P**
109859-58-7P 109859-59-8P 109859-68-9P
109859-78-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiischemia and antitachycardia agent)

RN 109859-50-9 CAPLUS

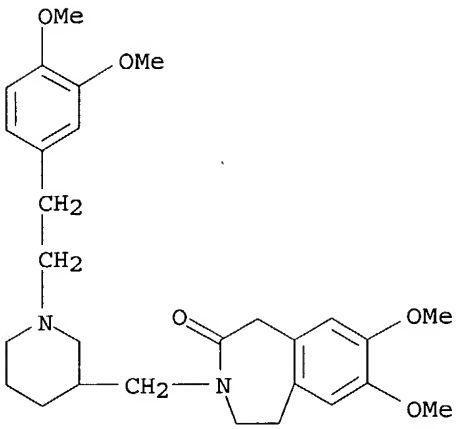
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)



RN 109859-52-1 CAPLUS

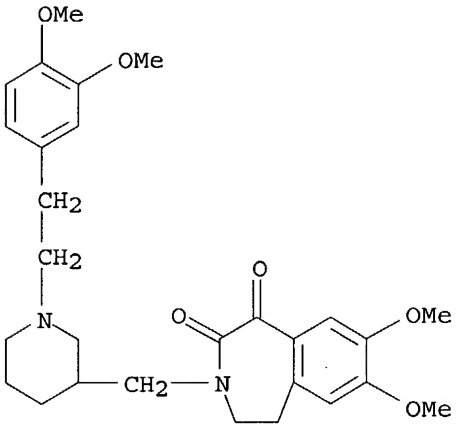
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-7,8-dimethoxy-, monohydrobromide

(9CI) (CA INDEX NAME)

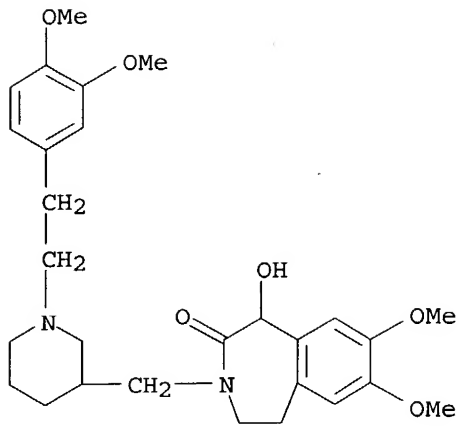


● HBr

RN 109859-57-6 CAPLUS
CN 1H-3-Benzazepine-1,2(3H)-dione, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-4,5-dihydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)

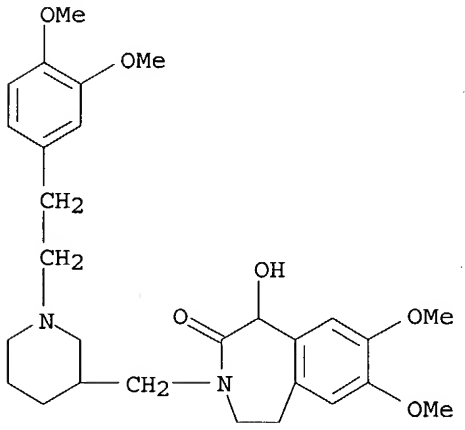


RN 109859-58-7 CAPLUS
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-1-hydroxy-7,8-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 109859-59-8 CAPLUS
CN 2H-3-Benzazepin-2-one, 3-[[1-[2-(3,4-dimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-1,3,4,5-tetrahydro-1-hydroxy-7,8-dimethoxy- (9CI) (CA INDEX NAME)



RN 109859-68-9 CAPLUS
CN 2H-3-Benzazepin-2-one, 1,3,4,5-tetrahydro-7,8-dimethoxy-3-[[1-[2-(3,4,5-trimethoxyphenyl)ethyl]-3-piperidinyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)